REMARKS

I. Petition for Extension of Time

Applicants herewith petition the Commissioner for Patents to extend the time for response to the Office action mailed January 11, 2005 for one month to May 11, 2005. Authorization is given to charge the extension of time fee of $120.00 (37 C.F.R. §1.136 and §1.17) to Deposit Account No. 23-1703. Any deficiency or overpayment should be charged or credited to the above numbered deposit account.

II. Claim Amendments

The Examiner is respectfully requested to exercise her discretion and enter this Amendment after final rejection.

Claim 1 has been amended to clarify that the core excipient, i.e., one or more alkaline additives, is a neutralizing agent present in the core in a sufficiently high amount. Specifically, claim 1 has been amended to recite that the neutralizing agent is present in an amount of approximately 10-35% by weight of the core material excluding the weight of an optional starter seed. Support for the amendment is provided by the specification at page 4, lines 10-15, where it is stated that "[t]he alkalizing agent in the core material will neutralize the absorbed acidic fluid and protect the active ingredient against degradation" and at page 6, line 27, where the amount of neutralizing agent is disclosed.

Claim 1 has been further amended to recite that the semipermeable membrane "consists of", as opposed to consists essentially of, the recited ingredients.

Claims 6, 12, 14, and 15 have been amended to recite -- starter seed --, as opposed to "sugar sphere", in view of the antecedent basis provided by amended claim 1. Support is found at page 5, line 21 of the specification, which provides that the core material may be produced with starter seeds. New claim 29 is supported by the specification at page 5, lines 19-21.

Applicants submit that no new matter has been introduced by any of the claim amendments.

III. Claim Rejections – 35 U.S.C. §103(a)

A. US 6,245,351 to Nara et al. ("Nara")

Claims 1, 3, 6-18, 20 and 25-28 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over US 6,245,351 to Nara et al. ("Nara"). The claims haven been amended to clarify the patentably distinguishing features of the claimed invention over Nara.

1. Nara does not recognize the need for a neutralizing agent in the core comprising an acid-labile active ingredient.

The active ingredient of the claimed dosage is an acid-labile substance, e.g., omeprazole. Amended claim 1 recites that the core incipient, i.e., one or more alkaline additives, is a neutralizing agent present in a sufficiently high amount (specification at page 4, lines 10-15). Advantageously, the neutralizing agent acts to neutralize acidic gastric fluids adsorbed through the semipermeable membrane while the dosage form, ***which is not enteric coated***, passes through the stomach en route to the small intestine. To effectively counter the absorbed acidic fluid and protect the acid-labile drug, the neutralizing agent must be present in a sufficiently high amount to protect the acid-labile, active ingredient against degradation, e.g., preferably 10 to 35% by weight calculated on the weight of the core material excluding the weight of an optional starter seed (specification at page 6, line 27).

Nara does not suggest the inclusion of a neutralizing agent in the core. This is no surprise since Nara discloses a broad range of other possible active ingredients (col. 3, lines 35-63), including omeprazole and lansoprazole, without giving any attention to or recognition of the unique problems relating to formulation of dosage forms having an acid-labile substance as the active ingredient. These formulations problems become even more complicated for acid-labile drugs when the dosage form is not enteric coated. Such formulation concerns may be irrelevant with opioid compounds which are expressly preferred by Nara (col. 3,lines 65). It is evident, therefore, that Nara fails to recognize the unique formulation problems associated with acid-labile drugs and the need to protect the acid-labile drugs from the acidic environment of the stomach, especially when the dosage form is not enteric coated.

Nara discloses the possibility of including a lubricant , such as talc, in the core (col. 5, lines 51-53). However, Nara does not expressly disclose the amount of lubricant to be present in

the core. Applicants submits that the person of ordinary skill in the art of pharmaceutical formulations would know that the amount of lubricant in the core of a dosage form is less than the high amount of neutralizing agent, e.g., preferably 10 to 35% required by the claimed invention. As part of this communication, Applicants are submitting a copy of page 328 from "The Theory and Practice of Industrial Pharmacy", Third Edition (1986) which discloses that talc, when used as a glidant or flow promoter, is typically present in a formulation at a 5% concentration. As such, the optional inclusion of a lubricant in the core as disclosed by Nara is different from the function of the neutralizing agent which is present in a sufficiently high amount in the core of the claimed invention.

The inclusion of a neutralizing agent in the core of the claimed invention provides a superior advantage over the composition disclosed by Nara when the core material comprises an acid-labile substance and the dosage form is not enteric coated..

2. The semipermeable membrane of the claimed invention does not contain a hydrophilic substance and swellable agent as disclosed by Nara.

Claim 1 has been further amended to recite that the semipermeable membrane "consists of", as opposed to consists essentially of, the recited ingredients. Thus, the semipermeable membrane of the claimed invention is defined by a water-insoluble polymer and a modifying agent. In contrast, the coating composition disclosed by Nara contains a hydrophilic substance and a swellable agent, both of which are excluded from the semipermeable membrane of the claimed invention.

Therefore, it is the swelling agent in the core of the claimed invention that expands upon exposure to the fluid or moisture absorbed through the semipermeable membrane (specification at page 4, lines 15-19). After a pre-determined time interval, the expansion of the swelling agent in the core of the claimed invention leads to a disruption of the semipermeable membrane by the built-up pressure. As such, the semipermeable membrane of the claimed invention disrupts notwithstanding the absence of a swelling agent in the membrane as required by Nara.

3. The composition, structure and release mechanism of the claimed dosage form are different and not suggested by Nara.

Advantageously, the core material of the claimed dosage form includes a neutralizing agent in a sufficiently high amount to protect the acid-labile active ingredient from degradation. Nara does not recognize or acknowledge the unique problems relating to formulation of a dosage form, ***which is not enteric coated***, having an acid-labile substance as the active ingredient. Finally, release of the active ingredient of the claimed invention is achieved without the presence of a swelling agent in the semipermeable membrane as required by Nara. Rather, the swelling agent present in the core of the claimed dosage form expands which leads to a disruption of the semipermeable membrane by the built-up pressure.

For all of the foregoing reasons, therefore, Applicants respectfully submit that the structure and advantages of the claimed invention formulation are not suggested by Nara. Withdrawal of the §103 rejection based on Nara is requested.

B. Nara in view of WO 98/54171

Claims 4, 5 and 23-26 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Nara in view WO 98/54171 in the name of Cotton et al. ("Cotton").

As stated by the Examiner on page 4 of the Office Action, Cotton is cited for the disclosure of the magnesium salt of S-omeprazole as an active ingredient.
Applicants submit that Cotton does not over come the deficiencies of Nara to suggest the claimed invention for the reasons given in the preceding Section. Withdrawal of the §103 rejection based on Nara in view of Cotton is requested.

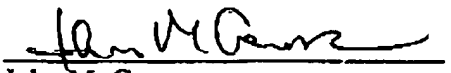
CONCLUSION

Applicants have made a good faith attempt to respond to the Office Action. It is respectfully submitted that claims 1, 3-10, 12-18, 20 and 23-29 are in condition for allowance, which action is earnestly solicited.

Any fees due in connection with this response should be charged to Deposit Account No. 23-1703.

Dated: 29 April 2005

Respectfully submitted,



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Enclosure (4pages): The Theory and Practice of Industrial Pharmacy, Third Edition (1986), p .328